CLAIMS

Claims 1-35 (canceled)

Claim 36 (currently amended): A method of repairing a diseased or injured tissue in a patient, comprising the steps of surgically obtaining a healthy chondrocyte specimen from ~~a non-diseased or injured part of~~ a patient's body, rapidly growing high-quality chondrocytes externally of the patient's body in spinner culture on microcarrier particles, and surgically implanting the rapidly grown high-quality chondrocytes into diseased or injured tissue of the patient's body, such that the high-quality chondrocytes regenerate within the patient's body, thereby producing a long-term cure of the patient's diseased or injured tissue.

Claim 37 (previously amended): The method of claim 36, wherein the healthy chondrocyte specimen is taken from the patient's nasal septal cartilage.

Claim 38 (original): The method of claim 36, wherein the rapidly grown high-quality chondrocytes are implanted for orthopedic purposes.

Claim 39 (original): The method of claim 38, wherein the implantation is in the patient's knee.

Claim 40 (currently amended): The method of claim 36, wherein the high-quality chondrocytes are grown in ~~spin-culture~~ spinner culture on microcarrier particles in a reduced oxygen environment.

Claim 41 (currently amended): The method of claim 40 in which the ~~low oxygen~~ reduced oxygen environment contains about 5% oxygen.

Claim 42 (original): The method of claim 36, wherein the microcarrier particles are composed of a biodegradable and biocompatible material.

Claim 43 (previously amended): The method of claim 42, wherein the biodegradable and biocompatible material is selected from collagen, dextran, N,N-diethylaminoethyl (DEAE)-dextran, or N,N,N-trimethyl-2-hydroxy-aminopropyl-dextran.

Claim 44 (original): The method of claim 42, wherein the biodegradable and biocompatible material is a cross-linked polymer prepared by crosslinking a polysaccharide with a polyamine.

Claim 45 (original): The method of claim 44, wherein the polysaccharide is selected from the group consisting of dextran, arabinogalactan, pollulan, cellulose and amylose.

Claim 46 (original): The method of claim 44, wherein the crosslinking polyamine is selected from a group consisting of lysine, ethylenediamine, alkylenediamine, phenylenediamine, xylenediamine, polyethylenimine, gelatin, albumin and fibrinogen.

Claims 47 - 57 (canceled)

Claim 58 (previously amended): A method of repairing a diseased or injured tissue in a patient, comprising the steps of surgically obtaining a healthy tissue specimen from a patient's body, rapidly growing high-quality cells from the tissue specimen externally of the patient's body in spinner culture on microcarrier particles, and surgically implanting the rapidly grown high-quality cells into diseased or injured tissue of the patient, such that the high-quality cells

regenerate within the patient's body, thereby producing a long-term cure of the patient's diseased or injured tissue.

Claim 59 (previously amended): The method of claim 58, wherein the healthy tissue specimen is taken from the patient's bone marrow, periosteum, perichondrium, cartilage, bone, or peripheral blood.

Claim 60 (previously amended): The method of claim 58, wherein the healthy tissue specimen is taken from the patient's bone marrow.

Claim 61 (original): The method of claim 58, wherein the cells are selected from a group consisting of chondrocytes, oesteoblasts, oesteocytes, chondrogenic cells, pluripotential cells, progenitor mesenchymal cells, fibroblasts, and mucosal cells.

Claim 62 (original): The method of claim 58, wherein the rapidly grown high-quality cells are implanted for orthopedic purposes.

Claim 63 (original): The method of claim 58, wherein the rapidly grown high-quality cells are implanted for orthopedic purposes.

Claim 64 (previously amended): The method of claim 58, wherein the high-quality cells are grown by spinner culture on microcarrier particles in a reduced oxygen environment.

Claim 65 (original): The method of claim 64 in which the low oxygen environment contains about 5% oxygen.

Claim 66 (original): The method of claim 58, wherein the microcarrier particles are composed of a biodegradable and biocompatible material.

Claim 67 (previously amended): The method of claim 66, wherein the biodegradable and biocompatible material is selected from collagen, dextran, N,N-diethylaminoethyl(DEAE)-dextran, or N,N,N-trimethyl-2-hydroxy-aminopropyl-dextran.

Claim 68 (original): The method of claim 66, wherein the biodegradable and biocompatible material is a cross-linked polymer prepared by crosslinking a polysaccharide with a polyamine.

Claim 69 (original): The method of claim 68, wherein the polysaccharide is selected from the group consisting of dextran, arabinogalactan, pollulan, cellulose and amylose.

Claim 70 (original): The method of claim 68, wherein the crosslinking polyamine is selected from a group consisting of lysine, ethylenediamine, alkylenediamine, phenylenediamine, xylenediamine, polyethylenimine, gelatin, albumin and fibrinogen.

Claims 71-83 (canceled).

Claims 36-46 and 58-70 all the claims in this application stand finally rejected.

Comments on Claim Objections

Claim 40 has been amended to be consistent with claim 36.

Claim 41, line 1 "low" has been changed to -- reduced -- as suggested by the Examiner.

Comments on Claim Rejection Under 35 USC § 112

Claim 36 has been amended by eliminating the expression "a non-diseased or injured part of"; and the claim now employs the same language as non-rejected claim 58. In view of the amendment, the rejection of claim 36 should be withdrawn.

Claim Rejection - 35 U.S.C. § 103

Claims 36-39, 42-46, 58-63 and 66-70 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over *Glorioso et al* in view of *Frondoza et al*, *Schinstine et al* and *Cherksey* and if necessary, in view of Armstrong.

In applicants' response of January 26, 2005, applicants argued that *Frondoza et al* cannot be combined with *Glorioso et.al* because *Glorioso et al* employ transfected cells and *Frondoza et al* employ unaltered cells; and to combine *Frondoza et al* and *Glorioso et al* would amount to making a rejection using non-analogous art.

In the official action of May 3, 2005, the Examiner stated that "expressing the protein by transfection would not alter the behavior of a chondrocyte in spinner culture". To rebut the position of the Examiner, applicants submit herein a declaration from Dr. Carmelita Frondoza, who by training and experience qualifies as an expert. In the declaration, Dr. Frondoza declares

that,

> although *Frondoza et al* and *Glorioso et al* both employ chondrocytes in their methods, the fact that *Glorioso et al* employs transfected chondrocytes as opposed to natural chondrocytes would render the *Glorioso et al* chondrocytes non-analogous and lacking in equivalency. This is so because introducing a DNA sequence (transfection) into a chondrocyte would have the effect of rendering the phenotype characteristic of the cultured chondrocyte unpredictable and would render the growth pattern (phenotype) of the chondrocyte during culture to be unpredictable.

In view of this declaration, it is believed that the rejection of the claims employing *Frondoza et al* in view of *Glorioso et al* should be withdrawn; and the same is requested.

Regarding *Cherksey*, applicants do not challenge the fact that cells have been cultured on a support matrix and transplanted.

Regarding Armstrong, applicants do not challenge the fact that cells have been cultured on microcarriers.

It is not seen that *Schinstine* can be combined with *Frondoza* and *Glorioso* to make a valid rejection because the *Schinstine* cells are cells which have been altered by treatment that inhibits cell proliferation. This process (inhibition of cell proliferation) is contrary applicant process in that applicants employ untreated, normal cells in their process. In view of the above remarks, combining *Schinstine* with *Frondoza* and *Glorioso* amounts to combining non-analogous art, which makes for an improper rejection.

Regarding the rejection of claims 40, 41, 64 and 65 employing *Starling et al.* Applicants traverse this rejection. These claims require spin-culture on microcarrier particles in a reduced

oxygen environment (claims 40 and 64) and in an oxygen environment of about 5% oxygen in claims 41 and 65. It is true that *Starling* cultures in a "carbon dioxide incubator", however, *Starling* is silent as to any amount of oxygen present in the culture. Clearly, claims 41 and 65 are not properly rejected employing *Starling* since no amounts of oxygen are set forth in the reference. Secondly, *Starling* is silent as to the presence of oxygen; and accordingly there would be no way of knowing the amount of oxygen in the "carbon dioxide incubator" or whether the oxygen was actually reduced therein. And finally and most importantly, *Starling* cultures on *Petri* dishes; this is a method contrary to applicants' spin-culture which purposefully seeks to avoid static *Petri* dish culture as used by *Starling*.

In view of the arguments herein presented and the Frondoza declaration, it is requested that all rejections under 35 USC § 103 be withdrawn.

Double Patenting

Claims 36-39, 42-46, 58-63 and 66-70 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,378,427 B1 or claims 1-9 of U.S. Patent No. 6,662,805 B2 in view of *Frondoza et al.*

Claims 40, 41, 64 and 65 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,378,427 B1 or claims 1-9 of U.S. Patent No. 6,662,805 B2 in view of *Frondoza et al* as set for above, and in further view of *Starling et al.*

Claims 36-46 and 58-70 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 10/654,057 or claims 1-35 of copending Application No. 10/066,992.

Claims 36-39, 42-46, 58-63 and 66-70 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-51 of copending Application No. 09/825,632.

Claims 40, 41, 64 and 65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-51 of copending Application No. 09/825,632.

Regarding the obviousness double patenting rejections applicants present herein a terminal disclaimer.

The provisional double patenting rejections are duly noted and a Terminal Disclaimer is being held in abeyance pending the finding of allowable subject matter in the pending applications.

Justification for Amendment After Final Rejection

Claim amendment after final rejection was required to correct formal matters. The amendment did not go to the merits of the case.

The Frondoza declaration under 37 CFR § 1.132 is being submitted herein to respond to the Examiner's position taken in the Final Rejection. Applicants have not been dilatory.

All objections and rejections have been addressed by applicants. It is requested that the Examiner find allowable subject matter in this application.

Sincerely,

July 18, 2005
Date

Sam Rosen
Reg. No. 37,991
Attorney for Applicant

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